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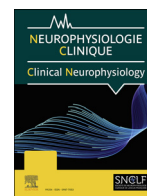
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Original article

Effects of home-based EEG neurofeedback training as a non-pharmacological intervention for Parkinson's disease



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ABSTRACT

Objectives: Aberrant movement-related cortical activity has been linked to impaired motor function in Parkinson's disease (PD). Dopaminergic drug treatment can restore these, but dosages and long-term treatment are limited by adverse side-effects. Effective non-pharmacological treatments could help reduce reliance on drugs. This experiment reports the first study of home-based electroencephalographic (EEG) neurofeedback training as a non-pharmacological candidate treatment for PD. Our primary aim was to test the feasibility of our EEG neurofeedback intervention in a home setting.

Methods: Sixteen people with PD received six home visits comprising symptomology self-reports, a standardised motor assessment, and a precision handgrip force production task while EEG was recorded (visits 1, 2 and 6); and 3 × 1-hr EEG neurofeedback training sessions to suppress the EEG mu rhythm before initiating handgrip movements (visits 3 to 5).

Results: Participants successfully learned to self-regulate mu activity, and this appeared to expedite the initiation of precision movements (i.e., time to reach target handgrip force off-medication pre-intervention = 628 ms, off-medication post-intervention = 564 ms). There was no evidence of wider symptomology reduction (e.g., Movement Disorder Society Unified Parkinson's Disease Rating Scale Part III Motor Examination, off-medication pre-intervention = 29.00, off-medication post intervention = 30.07). Interviews indicated that the intervention was well-received.

Conclusion: Based on the significant effect of neurofeedback on movement-related cortical activity, positive qualitative reports from participants, and a suggestive benefit to movement initiation, we conclude that home-based neurofeedback for people with PD is a feasible and promising non-pharmacological treatment that warrants further research.

Introduction

Idiopathic Parkinson's disease (PD) is a neurodegenerative condition that impairs motor function. PD is the second most common cause of

chronic neurological disability after stroke, affecting 1.5 % of people aged over 70 years [48]. Its main motor symptoms include akinesia (loss or impairment of voluntary movement), bradykinesia (fatigable slowness of movement), resting tremor, rigidity, and loss of postural reflexes

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[19]. The pathophysiology of PD is characterised by the progressive decay of dopamine-producing neurons in the substantia nigra region of the brain [45]. Dopaminergic medication (e.g., levodopa and dopamine agonists) is typically deployed to alleviate some of the motor symptoms of PD [42]. However, people with PD can show variations in response and prolonged pharmacological treatment is often associated with motor (e.g., involuntary movements known as dyskinesias) and psychiatric (e.g., confusion, hallucinations, apathy and somnolence) side-effects [22]. For instance, up to 40 % of people with PD may be affected by dyskinesia after 4 to 6 years of levodopa (L-Dopa) treatment [1]. The combination of drugs and disease progression may trigger apathy and somnolence in up to 20 % and 50 % of people with PD, respectively [4,47]. Moreover, pharmacotherapy dosages must be increased over time to maintain effectiveness [25], which may further increase the risk for developing side effects. These dose-limiting effects underscore a pressing need for the development of sustainable, non-pharmacological approaches, such as neuromodulation techniques, to manage motor symptoms of PD. However, studies of effective non-pharmacological treatments are very limited [2].

Non-invasive neurofeedback training is a personalised, non-pharmacological intervention that aims to enable individuals to modulate their brain activity [55]. With a lower likelihood of side-effects, when compared to pharmacological treatments, neurofeedback training is a possible alternative or adjunct to medication, with the potential to improve the quality of life for people with PD [14]. Initial studies have employed real-time functional magnetic resonance imaging (rt-fMRI) neurofeedback combined with motor imagery with the aim of training people with PD to increase the activation of the supplementary motor area (SMA) [60,61], a cortical brain region that shows reduced activation in people with PD during preparation and execution of voluntary movements [18,36]. Participants received two [60] or three [61] neurofeedback training sessions consisting of 2×6.5 min [60] or 4×3 min [61] neurofeedback blocks. They were asked to imagine movements to develop a strategy that enabled them to fill as many bars as they could on an on-screen thermometer, reflecting their real-time SMA activation (more bars filled = greater activity). Results revealed that SMA activation increased from a neutral fixation cross baseline to the neurofeedback blocks, and the interventions were associated with significant pre- to post-training reductions in PD motor symptoms (e.g., 4.5 – 5.2 point improvements on the Movement Disorders Society Unified Parkinson's Disease Rating Scale) [60,61]. However, limitations of this approach include the need for access to an MRI scanner, its high costs, as well as contraindications (e.g., exclusion of people who have ferromagnetic implants). In contrast, scalp-based electroencephalography (EEG) is cheaper, has essentially no contraindications and is widely available in neurological health care settings. Crucially, the portability of EEG presents opportunities for decentralised clinical trials such as home-based EEG neurofeedback treatment, which may aid recruitment and retention [50]. Moreover, decades of observational and intervention studies that employed EEG recordings in people with PD provide observational and mechanistic insights that can inform the choice of a suitable EEG neurofeedback target signal [38].

Standout candidates for EEG neurofeedback training in PD are oscillations in the beta spectral power band (around 13–30 Hz) and in the mu rhythm (around 8–12 Hz) [38]. A case for targeting beta oscillations can be drawn from studies of people with PD who have undergone functional neurosurgery for deep brain stimulation (DBS). DBS studies typically reveal exaggerated beta activity in the subthalamic nucleus (e.g., [8]) and show that DBS stimulation can suppress beta activity, which correlates with improvements in bradykinesia [32]. However, when focusing on non-invasive scalp-based EEG studies (the most relevant for home-based EEG neurofeedback), the most consistent finding related to movement impairment in people with PD concerns the mu rhythm, specifically, mu event-related desynchronization (ERD) [34]. Mu ERD refers to a notable reduction in power around 8–12 Hz (also known as alpha ERD) that specifically emerges at central electrode locations overlying

the primary motor areas of the cortex, and which immediately precedes voluntary movement [38]. It is triggered by dopaminergic drive to the basal ganglia promoting excitatory cues to the SMA, while PD is characterized by the progressive degeneration of these crucial motor circuits resulting in impaired motor programming and, in extreme cases, akinesia [34]. As a result, people with PD show attenuated mu ERD at contralateral sensorimotor areas (i.e., C3 or C4) compared to healthy controls [12]. Importantly, dopaminergic medication helps to restore mu ERD amplitudes [13,36] and mu ERD correlates with improved bradykinesia symptoms [64]. Further, DBS studies that targeted the subthalamic nucleus in combination with L-Dopa have shown an increase in mu ERD latency during movement preparation and an increase in mu ERD during movement execution over central electrodes [12]. Taken together, we deduce that: a) there is a strong mechanistic rationale for interventions that can restore some activation to the key basal ganglia to SMA movement circuits in people with PD; b) empirical findings demonstrate that mu ERD, particularly at electrode sites overlying contralateral sensorimotor areas (e.g., C3 electrode for right hand movements, C4 electrode for left hand movements), is a key determinant of the preparation and initiation of movement; c) PD disrupts “normal” mu ERD, and this could explain movement difficulties; and d) current pharmacological therapy can restore “normal” mu ERD and motor performance. Based on this evidence, mu ERD over the motor cortex is considered an ideal target for neurofeedback treatment designed to activate key SMA motor circuits with the goal of improving motor impairment in PD.

Importantly, research in healthy controls has established that mu ERD is trainable via relatively brief neurofeedback interventions. For example, healthy participants were able to exert some control over their mu ERD after just 30-mins of mu neurofeedback training [54]. This was associated with an immediate benefit in cognitive (serial-sevens accuracy) and motor (timed-up-and-go test) performance [54]. Another study provided 3-hrs of mu ERD training to healthy participants and found a strong and enduring training effect where participants were able to reduce their pre-movement mu activity for at least a few days after the feedback was withdrawn [49]. Surprisingly, however, only a handful of exclusively laboratory-based studies attempted scalp-based EEG neurofeedback for PD, as described in detail in recent reviews [3,14,38]. Although these preliminary studies provide some initial evidence for the feasibility of EEG neurofeedback training in people with PD in a laboratory setting, they have been largely inconclusive due to insufficient clinical information (e.g., assessing/reporting symptom changes), very small sample sizes (mostly case studies), only single training sessions, and lack of inferential statistical testing [3]. Crucially, the choice of neurofeedback target varied between (and in some cases, within) previous studies, with none of them targeting mu ERD despite the compelling case for this neurofeedback target. Given the initial feasibility of mu ERD neurofeedback training in healthy participants and the therapeutic potential of mu ERD neurofeedback training for PD, we aimed to test the feasibility of mu rhythm EEG neurofeedback training in people with PD in the present study.

We took several steps to provide a highly original and rigorous examination of EEG neurofeedback in PD. First, based on a thorough review of previous literature, we identified mu ERD as an evidence-based target for training [38]. Second, our design was informed by studies that successfully trained mu ERD in healthy participants [49,54]. Third, the details of our study were pre-registered (<https://www.isrctn.com/ISRCTN16783092>). Fourth, we evaluated our protocol in accord with the recent consensus on the reporting and experimental design of clinical and cognitive-behavioural neurofeedback studies (CRED-nf) checklist (see supplementary material), to help promote robust experimental design and transparent reporting [51]. Finally, and most importantly, the present experiment was designed to deliver the neurofeedback intervention in participants' homes, making it the first examination of portable, home-based neurofeedback treatment in PD.

The primary aim of the study was to test the feasibility of our neurofeedback intervention in a home setting. We hypothesized quadratic

effects over three home visits that comprised the test phase of our study. Specifically, we expected that spectral power in the mu band at central electrodes would be greater, indicative of impaired mu ERD, during an (off-medication) pre-test B compared to an (on-medication) pre-test A, and we predicted that this difference would normalise to some degree during the (off-medication) post-test following a period of neurofeedback training. This pattern would provide novel evidence of learned self-regulation via home-based training. Motor performance and symptomology were our secondary outcomes. We explored whether these were characterised by similar levels in pre-test A and post-test, and worse motor performance and more severe symptomology in pre-test B. Such findings would evidence an ability of mu ERD neurofeedback training to yield similar outcomes to PD medication. We further hypothesised linear effects over three home visits that comprised the neurofeedback training phase of the study, characterised by a decrease in mu power and an improvement in motor performance from one training session to the next. Finally, as this is the first study of EEG neurofeedback in participant homes, we also assessed the qualitative experience of participants via a brief interview.

Methods

Protocol registration and governance

The methodology, hypotheses, sampling plan, primary and secondary outcomes were prospectively registered on 29th August 2017 (<https://www.isrctn.com/ISRCTN16783092>). The trial was overseen by a steering group comprising the research team, an independent clinician, and members of the PD community. Local people with PD were key panel members who generously gave their time to attend meetings, provide feedback on the protocol and participant facing materials, volunteer as pilot participants, raise awareness of the project in the PD community and provide advice on follow-up plans. They expressed great enthusiasm for non-pharmacological PD research and a keen desire to help the research team to conduct and publish this experiment for benefit of the wider PD community.

Recruitment and sampling plan

Recruitment to the study was initiated by members of the clinical research team who were involved in Movement Disorders Clinics and Parkinson's Support Groups in the local health board, and who were familiar with study inclusion/exclusion criteria (Table 1) in order to provide initial eligibility assessments. This led to 31 potential participants being identified and consenting to a follow-up conversation with the lead researcher. Four of the potential participants did not respond to the researcher follow-up contact, and four withdrew their interest after contact was made. The remaining 23 potential participants agreed to join a recruitment list to take part in the study. Of these, seven participants were unable to sign-up within the data collection window (e.g., due to illness, personal circumstances or participation in another study); the remaining 16 signed-up and participated in the study. Hence, our sampling plan was based on the number of people with PD we could contact, enrol and who could complete the study within a 7-month data collection period [33].

Participants

Sixteen (10 male, 6 female; $M_{\text{age}} = 67.31$, $SD = 9.77$ years) participants in the early stage of PD (Hoehn and Yahr stage 1–2; $M_{\text{years since diagnosis}} = 5.06$) consented to take part. Fourteen of the participants were receiving treatment with L-Dopa and two participants were receiving other Parkinsonian medication. Importantly, there was no change in medication dosage over the course of the experiment. The experiment received favourable opinions from both the University (reference 16–15,660) and the National Health Service Health Research Authority

Table 1

Participant inclusion and exclusion criteria.

Inclusion Criteria	Exclusion Criteria
1. Idiopathic PD diagnosed using the UK Brain Bank Diagnostic Criteria	1. Clinical diagnosis of dementia
2. Hoehn and Yahr stage 1–3	2. Active psychosis, clinically significant depression or behavioural disturbance
3. On stable treatment for the past month and no planned changes over the period of the study	3. Presence of another neurological condition
4. Ability to give informed consent	
5. Aged over 18 years	

(reference 16/WA/0115) research ethics committees. All participants provided informed consent before taking part. A sensitivity analysis with G*Power 3.1 and its default settings for within-factor effects of a repeated measures analysis of variance (ANOVA) [15] indicated that a sample size of 13 to 15 (to account for occasional missing data – see statistical analysis section below) would allow detecting within-participant changes of $f = 0.35 - 0.38 / \eta_p^2 = 0.62 - 0.68$ (i.e., large size effects [9]) with 80 % power for a 3-level repeated measures ANOVA at an alpha level of 0.05. While there are no previous studies of ERD neurofeedback in PD, previous studies of a) the effects of L-Dopa medication on mu ERD in PD [13] and b) the effects of mu ERD neurofeedback in healthy controls [49], have revealed large effects for within-person changes in cortical activity (our key index of neurofeedback feasibility).

Design

We employed a fully within-subjects design. Each participant received six home visits from a researcher, with each visit separated by a minimum of 48 hrs. Aside from this requirement, the scheduling of visits was deliberately flexible to accommodate the participant preferences. The most common inter-session-interval was 7 days and the total number of days required to complete all visits ranged from 19 to 60 days across participants. There were two distinct phases of the experiment. The “Test” phase of the experiment comprised home visits 1, 2 and 6. These visits are respectfully labelled as “pre-test A”, “pre-test B” and “post-test”. Participants were on their regular medication during pre-test A (i.e., on-medication) and refrained from taking their medication (overnight withdrawal) ahead of pre-test B (off-medication) and post-test (off-medication). In all visits comprising the Test phase, participants completed assessments of PD symptomatology and performed a force production task (see Precision Motor Task section below) while their cortical activity was measured. The “Training” phase of the experiment comprised home visits 3, 4 and 5. These visits are respectfully labelled as “neurofeedback session 1”, “neurofeedback session 2” and “neurofeedback session 3”. Participants refrained from taking their medication (overnight withdrawal) ahead of all neurofeedback sessions (i.e., off-medication). Each neurofeedback session comprised 12 × 5 min blocks of neurofeedback training, ensuring a total of 1 hr of neurofeedback training per each session. A schematic of the design is provided in Fig. 1, and a more detailed description of the neurofeedback session and block factors are provided in the “Neurofeedback Intervention” section below.

Precision motor task

During each visit in the Test phase of the experiment, participants performed 40 trials of a precision grip force task. Specifically, they used their dominant hand (right-handed $N = 14$, left-handed $N = 2$) to squeeze a handgrip dynamometer, with the goal of sustaining a force equivalent to 10 % of their maximum grip strength (i.e., maximum voluntary contraction; MVC) as accurately as possible for 5 s. Participants commenced each trial by squeezing the dynamometer to trigger a static yellow force line to

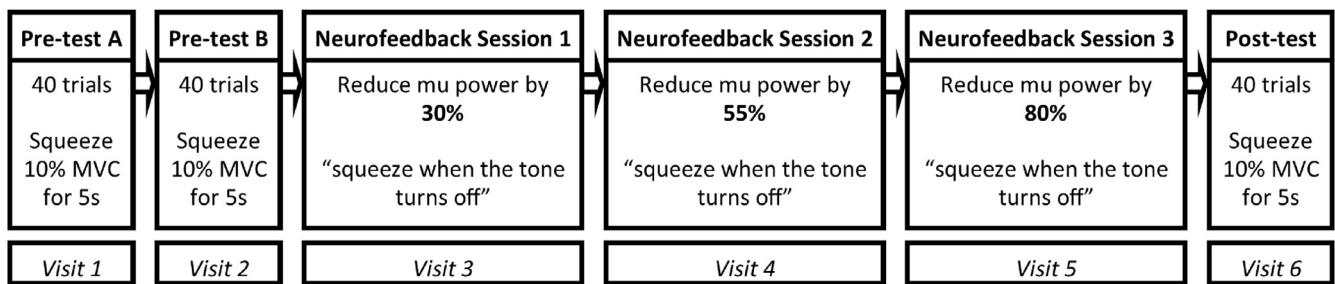


Fig. 1. Schematic of experiment design. All participants received six home visits, each separated by at least 48 hrs. The test phase of the experiment comprised visits 1, 2 and 6 and the neurofeedback training phase of the experiment occurred in visits 3, 4 and 5. The target reduction of alpha power was calibrated based on participants' resting state activity as measured at the beginning of Neurofeedback Session 1.

appear on a computer screen set at 10 % of their pre-established MVC. Once the yellow line appeared, participants had to adjust their current grip strength, which was depicted by a dynamic pink line on the screen, to trace the static yellow target line as closely as possible. Both lines remained on the screen for 5 s and then disappeared to indicate the end of the trial. Participants were asked to release their grip at the end of each trial, take a moment to re-focus, and then re-grip the dynamometer to commence the next trial as soon as they felt ready. This precision grip task is commonly used to assess fine motor control [6,10,41].

Neurofeedback intervention

During each visit in the training phase of the experiment, participants received 1 hr of neurofeedback training. At the beginning of the first neurofeedback session, baseline cortical activity was assessed from the C3 electrode site for right-handed participants and the C4 electrode site for left-handed participants. This baseline activity was later used to calibrate the target threshold of the subsequent neurofeedback training visits. Sites C3 and C4 are assumed to approximately correspond to the right- and left-hand motor area, respectively, within the primary motor cortex [65]. We focused our feedback at the C3 (C4 for left-handers) sites because the mu ERD measured over the primary motor cortex supports movement planning and fine motor control of the hands [11,38]. Additionally, an electrode was placed over the orbicularis oculi muscle of the left eye (right eye for left-handers) to remove eye-blink artefacts, with linked reference electrodes attached to the right and left mastoids and a ground electrode attached to FPz. Recordings were acquired by active electrodes connected to a wireless 4-channel neurofeedback system (Brainquiry PET-4, Nijmegen, The Netherlands). In tandem with cortical recordings, a computer running Bioexplorer software (Cyberevolution, U.K.) used a 6th order Butterworth infinite impulse response 9 to 11 Hz bandpass filter to extract power within the mu band from the EEG signal and fed this back to the participants in the form of an auditory tone [54]. Importantly, the tone was programmed to vary in pitch based on the level of mu power and silence completely when mu power was decreased by 30 % (neurofeedback training session 1), 55 % (neurofeedback training session 2) and 80 % (neurofeedback training session 3), relative to each participant's individual baseline cortical activity as acquired before the first training session.

These thresholds were based on previous research documenting similar decreases in EEG power during motor preparation [36], and confirmed via pilot testing which established that they were achievable during our brief intervention. As mu power is inversely related with cortical activity, the progressively more extreme thresholds were designed to encourage increased activation at the C3 (or C4) sites above the primary motor areas, which is characteristic of relatively autonomous and efficient motor preparation [11]. In addition to reducing mu power by the aforementioned thresholds, the system also required <10 μ V of 50 Hz activity in the signal (i.e., low mains noise) and the absence of eye-blinks, as detected by the electrode paced adjacent to the eye contralateral to the dominant hand (eye-blinks were detected as >75 μ V of

1–7 Hz activity at the eye-electrode), for the tone to silence. These control features helped ensure the signal was being regulated by cognitive processes and was not contaminated by electrical, muscular or eye-blink artefacts [49].

The auditory neurofeedback training was delivered to participants over 12 \times 5-min blocks, each separated by a 2-min break. Participants were seated in a comfortable chair in their home. Each time the thresholds described above were met, the auditory tone was set to silence for 1.5 s and participants were instructed to squeeze the handgrip dynamometer with their dominant hand to produce a grip force equivalent to 10 % MVC for 5 s (i.e., to initiate a trial of the precision motor task described in the section above). This instruction was designed to help participants associate the relative increase in cortical activation with the onset of movement.

Measures

Cortical Activity. EEG activity was recorded from the Fz, Cz, C3 and C4 sites on the scalp [23] during the test phase of the experiment, and from C3 (for right-handers) or C4 (for left-handers) during the neurofeedback training. Recordings were obtained via active electrodes connected to a DC amplifier (Brainquiry PET-4, The Netherlands), with linked reference electrodes attached to the right and left mastoids and a ground electrode attached to FPz. Recording sites were cleaned, abraded, and conductive gel (Signa gel, Parker, Biosense Medical, U.K.) was applied to ensure that electrode impedances were below 10k Ω . The signals were digitized at 24-bit resolution (Brainquiry, The Netherlands) and transmitted via Bluetooth at a sampling rate of 200 Hz to a computer running Bioexplorer (Cyberevolution, U.K.) software. We employed Butterworth infinite impulse response (6th order) bandpass filter at 9–11 Hz to extract EEG data from each recording.

Precision Handgrip Performance. Performance on the precision motor task was assessed in four ways. We recorded the time in milliseconds (ms) from the onset of each trial to the moment that the force produced by the participant arrived and remained between 9 % and 11 % of their MVC for 200 ms (i.e., time taken to get into the region of the 10 % target – Fig. 2). We interpret this time-based measure as an index of the participants' ability to plan the movement (e.g., [26,27]), with shorter times indicating more accurate pre-planning of force and, thus, better performance. We also recorded three error scores. Absolute error was the discrepancy (in% of MVC) between the target force and the produced force; this reflects accuracy (i.e., proximity to target). Constant error was similar, but with the sign of the error (negative for errors below target force and positive for errors above target force) factored in; this reflects bias (i.e., any tendency to undersqueeze or oversqueeze). Finally, variable error was the within-person standard deviation of constant error scores across trials; this reflects consistency (i.e., consistency of bias across trials). In all cases higher scores represent worse performance (i.e., greater error, greater bias, inconsistency) and scores of zero (no error, no bias, perfect consistency) are optimal. These measures were averaged during each trial, with the averaging commencing at the point

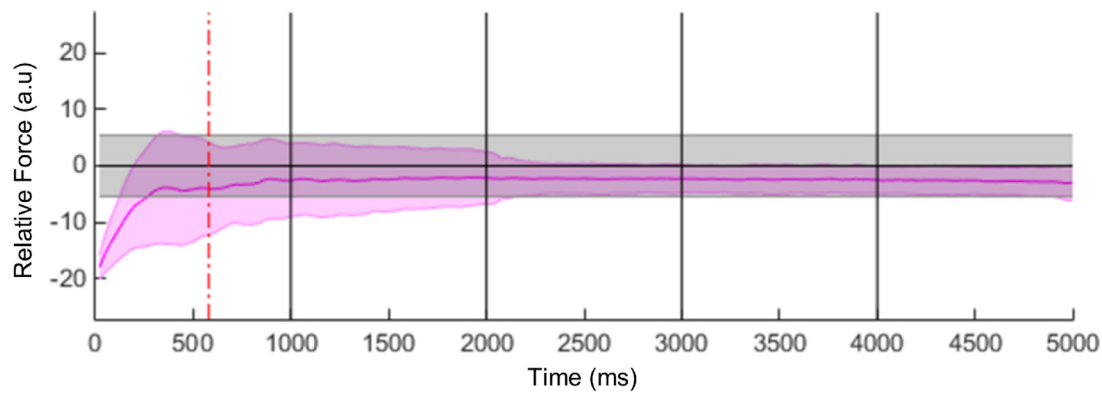


Fig. 2. Example force recording from our handgrip task. Solid pink line indicates force produced. Horizontal black line indicates target force (i.e., 10 % MVC). Shaded grey area indicates ± 1 % of target (i.e., 9–11 % MVC). Our time-based measure of movement planning was calculated as the time from the onset of each trial to the moment that the force produced arrived and remained between 9 and 11 % MVC for 200 ms, indicated by the dotted red line on this trace. Movement accuracy (absolute error) and bias (constant error) concerned the discrepancy between the produced force (pink line) and the target force (horizontal black line) while consistency (variable error) concerned the consistency of the produced force to target force discrepancies across trials. All error scores were computed from the dotted red line until the end of each 5 s trial.

at which participants' force arrived and remained between 9 % and 11 % of their MVC for 200 ms and terminating at the end of each 5 s trial (Fig. 2). These error measures thereby reflect the online component of movement control [26,27]. All performance measures were calculated for each trial and then averaged over the total number of trials per visit. This yielded a single score for each measure for each of the six experimental visits.

Motor Symptoms of PD: Self-reported. Participants' self-reported PD motor symptoms were measured using the Motor Aspects of Experiences of Daily Living (MEDL) questionnaire, which is Part II of the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) [16]. This subscale comprises 13 items enquiring about difficulties experienced during motor aspects of daily life (e.g., dressing; handwriting; turning in bed) during the past week, with items rated on a 5-point scale ranging from 0 (no problems) to 4 (severe problems). Responses to the 13 items are summed to yield a score ranging from 0 to 52, with higher scores indicating more severe symptomatology.

Motor Symptoms of PD: Observer rated. We also conducted an objective assessment of motor function using the Motor Examination that forms Part III of the MDS-UPDRS [16]. The experimenter, a trained MDS-UPDRS rater, observed participants as they engaged in 33 standardised tests (e.g., moving each arm from an outstretched position to the tip of the nose; rising from a chair; extending each arm and turning the hands from palm up to palm down), and rated the movements on a 5-point scale ranging from 0 (no problems) to 4 (severe problems). Scores for the 33 tests are summed to yield a total ranging from 0 to 132, with higher scores indicating more severe symptomatology.

Quality of Life. We assessed self-reported quality of life using the Parkinson's Disease Quality of Life Questionnaire (PDQ-8) [24]. Participants responded to eight items concerning how often during the past month they experienced certain feelings or symptoms (e.g., had difficulty getting around in public; felt embarrassed in public due to having Parkinson's disease) on a 5-point scale (0 = *Never*, 1 = *Occasionally*, 2 = *Sometimes*, 3 = *Often*, 4 = *Always*). Scores were summed, divided by the maximum possible score (32), and multiplied by 100 to yield a standardized score ranging between 0 and 100, where higher scores indicate lower quality of life.

Participant Acceptability. At the end of the final neurofeedback training session (neurofeedback session 3) we asked participants to verbally respond to the questions: a) "do you think the neurofeedback training has helped you to control your movements?"; b) "would you recommend this type of training to other people with PD?" and c) did you find any strategies to help you control the neurofeedback tone, and if so, what were they? and we recorded participants' responses with a Dictaphone.

These questions were expected to elicit a basic yes or no answer, which the researcher would then probe with stock follow-ups such as "can you explain why" and "can you give me an example of how" in a format that was designed to stimulate an organic discussion about these key aspects of the experience of home-based neurofeedback training among people with PD.

Procedure

After identifying potential participants (see Recruitment section above) a member of the research team visited each of the 16 individuals who ultimately became participants and they were fully briefed about the experiment before they provided informed consent, and home visits to conduct the experiment were arranged. Participants' general practitioners were also informed about the study participation and invited to contact the lead consultant on the research team if they had any questions or concerns; no such contacts were made.

Once consent was established, the researcher made six 2-hr visits to the home of each participant in order for them to complete both the test phase (visits 1, 2 and 6) and the neurofeedback training phase (visits 3, 4 and 5) of the experiment, with each visit separated by a minimum of 48 hrs (M inter-session-interval = 8.72 ± 3.84 days). The three visits comprising the test phase followed a common general procedure. First, participants were briefed, seated, and fitted with the EEG recording system. We prepared the skin by lightly abrading over the mastoids with exfoliating paste, and with a blunt needle at the scalp sites (Fz, Cz, C3, C4). The sites were then cleaned with an alcohol wipe, conductive gel was applied, and disposable spot electrodes (BlueSensor, Ambu, Denmark) were placed and secured using tape and a lycra cap. The EEG amplifier was attached by an elastic and Velcro strap to the participant's non-dominant arm. After instrumentation, we assessed the participant's MVC. Participants were given a handgrip dynamometer (MLT004/ST, AD Instruments, Australia) and they were asked to squeeze the dynamometer with their dominant hand as hard as they could, for a period of 3 s. This process was repeated five times, with a 1-min break to allow recovery between each maximal attempt. We recorded the biggest force generated during the five attempts as the MVC and used that force to calculate the 10 % MVC target for the subsequent precision handgrip task. The researcher entered the target threshold into a bespoke computer script designed to control the experiment (Visual Basic, Microsoft, U.S.A.) and after a short break, the participant was instructed about the precision handgrip task. Specifically, they were told that they would see a pink line on the screen, reflecting their grip force, and a static yellow target line, reflecting the target grip force, which was set at 10 % of their

MVC. They were further told that each time they squeezed the dynamometer, a trial would start, and their goal was to produce a force that ensured their pink line matched the yellow line as quickly as possible, and remained on the yellow line as closely as possible, for 5 s. At the end of each 5 s trial the screen would go blank, and they were to release their grip, re-focus, and commence the next trial whenever they felt ready. Their EEG was recorded continuously from trial 1 to trial 40, and participants were asked to remain still and quiet where possible for the duration of the 40 trials to help optimize the EEG recordings. Participants required an average of 7 mins 42 s ($SD = 1 \text{ min } 8 \text{ s}$) to complete the 40 trials of the handgrip task. After completing the handgrip task, the EEG hardware was removed, participants were asked to complete the MEDL and the PDQ-8 questionnaires, and the researcher took participants through the MDS-UPDRS Part III motor examination.

The three visits comprising the neurofeedback phase of the experiment adopted a general procedure as follows. First, participants were briefed, seated, and fitted with the neurofeedback system. Recording sites were prepared as described previously and electrodes were affixed at the locations described in the Neurofeedback Intervention section above. Next, we assessed the participant's baseline 9–11 Hz power by asking them to fixate on a cross displayed on a computer screen at eye level, for a period of 5 s. During this time, 9–11 Hz power was monitored. This process was repeated five times and the average was used as their baseline 9–11 Hz power value to calibrate subsequent neurofeedback training sessions. Baseline data was only applied in neurofeedback session one to ensure a comparability across training sessions. Having established individual baselines, the experimenter manually set the threshold for silencing the neurofeedback tone in the neurofeedback software. Participants were then instructed that in the next phase of the experiment they would hear a tone that was contingent on their brainwaves, and which would silence when they produced the type of brainwaves that we theorized would aid their movement. No explicit strategy was provided and participants were asked to try to identify successful regulation strategies (i.e., those that were followed by silenced tone). Further, participants were asked to squeeze the handgrip dynamometer at 10 % MVC for 5 s when the tone was silenced in order to associate reduced 9–11 Hz power (i.e., suppression of their mu rhythm; mu ERD) with the onset of movement. Participants completed the 12×5 -min blocks of neurofeedback training, with brief comfort breaks as required between each block. The neurofeedback hardware was removed at the end of the final neurofeedback block, and at the end of the final neurofeedback training session, participants were asked to verbally respond to the participant acceptability questions and we recorded their responses on a Dictaphone. At the end of the final home visit participants were thanked for a final time and invited to contact the experimenter for the results of the experiment at the end of the data collection period.

Statistical analyses

One participant withdrew from the experiment after pre-test B, and two participants had noisy EEG data for a portion of at least one of the test sessions; these EEG data were removed from the sample prior to analyses. This yielded a sample of 13 participants for EEG analyses during the test-phase, and 15 participants for EEG analyses during the training phase, and for all the remaining behavioural and self-report assessments.

Quantitative Analyses. We analysed our quantitative data during the test phase (EEG, precision handgrip performance, PD symptomology), the training phase (EEG, precision handgrip performance), and across the combination of phases to capture all six visits (EEG, precision handgrip performance). In the test phase we had a-priori expectations of quadratic effects (i.e., similar outcomes in pre-test A and post-test, and discrepant outcomes in pre-test B). Accordingly, we ran 3 Test (pre-test A, pre-test B, post-test) repeated measures Polynomial Trend ANOVAs with a focus on the quadratic outcomes. In the training phase we expected linear effects (e.g., progression from one training session to the

next). We therefore ran 3 Session (Neurofeedback Session 1–3) Polynomial Trend ANOVAs for our measures of handgrip performance and a 3 Session \times 12 Block (EEG during each 5-min block of training) Polynomial Trend ANOVA for cortical activity, with a focus on the linear outcomes. Although the training and test phases reflected distinct components of our experiment with subtly different procedures and predictions, for completeness, we also ran six-level repeated measures ANOVAs (i.e., pre-test A, pre-test B, neurofeedback session 1–3, post-test) for the EEG and performance measures. As we had no firm a-priori predictions about these six-level analyses, we report the univariate ANOVA outcomes, with the Greenhouse-Geisser correction procedure applied wherever the sphericity of variance assumption was violated. Finally, we computed the number of times the neurofeedback tone was silenced in each 5-min training block and subjected these data to a 3 (Session) \times 12 (Block) Polynomial Trend ANOVA. This measure reflects the real-time index of neurofeedback as provided to participants [51] with higher scores indicating better control of brainwaves. For brevity, the results of the tone silence analyses are reported in the supplementary online material.

Qualitative Analyses – Participant Acceptability. To assess participant acceptability, we initially counted the yes and no responses to the three verbal questions posed at the end of the final neurofeedback training session in order to compute the percentage of participants who: a) found the neurofeedback helpful; b) would recommend to others; and c) developed a strategy to control the neurofeedback tone. Participant responses to “how” and “why” questions that were posed to probe their initial yes or no responses were transcribed verbatim and then the lead author read the transcripts to immerse in the data and applied conventional thematic content analysis to generate themes to capture and summarize all types of view [20].

Results

Part A: quantitative

Cortical activity

Test Phase. Repeated measures Polynomial Trend ANOVAs performed for each recording electrode revealed significant quadratic effects at the C3 ($F(1,12) = 5.87, p = 0.03, \eta_p^2 = 0.33$) and the C4 ($F(1,12) = 5.50, p = 0.04, \eta_p^2 = 0.31$) sites, and directionally similar non-significant effects at Cz ($F(1,12) = 4.02, p = 0.07, \eta_p^2 = 0.27$) and Fz ($F(1,12) = 1.09, p = 0.32, \eta_p^2 = 0.09$). All sites were characterised by an increase in mu power from pre-test A to pre-test B, and then a decrease in mu power from pre-test B to post-test (Figs. 3A - 3D). This provides evidence that the neurofeedback intervention was successful in shaping participants' EEG mu activity in the prescribed manner at the targeted bilateral C3 and C4 sites.

Training Phase. The 3×12 Polynomial Trend ANOVA employed to analyse cortical activity during the neurofeedback training phase of the experiment revealed a significant linear effect for Session ($F(1,14) = 4.97, p = 0.04, \eta_p^2 = 0.26$), showing a decrease in C3 (C4 for left-handers) mu power from the first and second neurofeedback sessions to the third neurofeedback session ($M_{\text{session } 1} = 7.56 \mu\text{V}^2, M_{\text{session } 2} = 7.60 \mu\text{V}^2, M_{\text{session } 3} = 6.94 \mu\text{V}^2$ per block). This provides evidence for a between-session effect of the neurofeedback intervention; participants were most effective in suppressing their mu power in the final training session where the feedback threshold was the most severe (Fig. 3E). There was no significant linear effect for Block ($F(1,14) = 0.19, p = 0.67, \eta_p^2 = 0.01$) and there was no Session \times Block interaction, ($F(1,14) = 1.17, p = 0.30, \eta_p^2 = 0.08$). These data imply that our neurofeedback intervention was successful in encouraging self-regulation of mu activity, with adaptations occurring between, but not within, individual training sessions. Additional analyses based on the number of silenced tones revealed linear effects for Session and Block (see supplementary material).

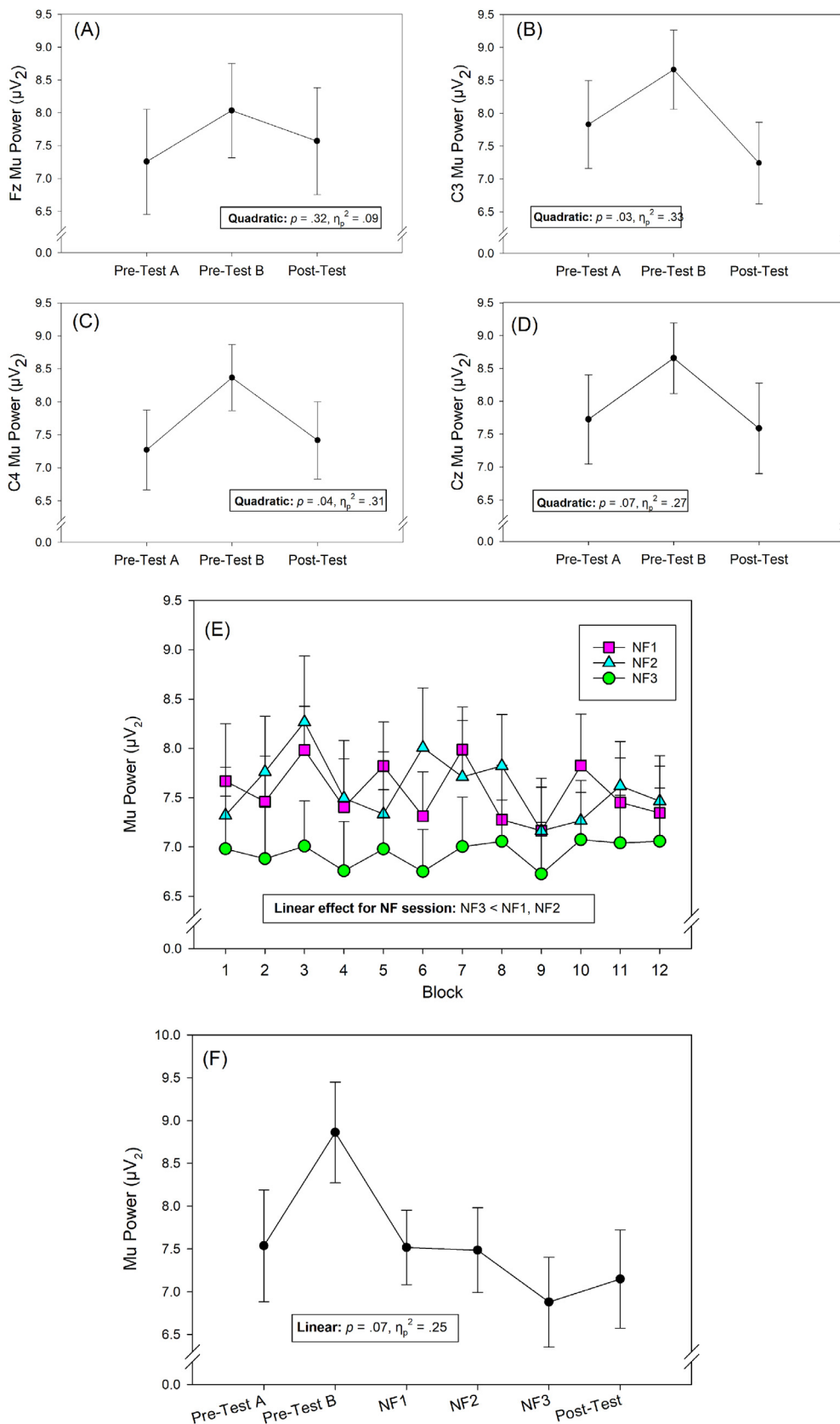


Fig. 3. Mean EEG mu power (9–11 Hz) recorded during the test phase of the experiment for different electrode positions (Panels A-D), the training phases of the experiment for EEG neurofeedback electrode position C3 (C4 in left handers – Panel E), and across all experimental visits for EEG neurofeedback electrode position C3 (C4 in left handers – Panel F). Pre-test A = on anti-Parkinsonian medication and before neurofeedback intervention. Pre-test B = off anti-Parkinsonian medication and before neurofeedback intervention. NF1, NF2 and NF3 = neurofeedback training sessions off anti-Parkinsonian medication. Post-test = off anti-Parkinsonian medication and after neurofeedback intervention. Error bars indicate standard error of the means.

All Visits. A six-level repeated measures ANOVA to compare μ power at the neurofeedback site over the six visits that comprised both the test and the training phase of the experiment revealed a significant effect of visit ($F(5,60) = 3.04, p = 0.04, \eta_p^2 = 0.20, \epsilon = 0.56$). This was characterized by a marginal linear trend ($F(1,12) = 4.00, p = .07, \eta_p^2 = 0.25$), where μ power tended to be greatest in pre-test B, and lowest in the final neurofeedback training session and the post-test (Fig. 3F).

Precision handgrip performance

Test Phase. Repeated measures Polynomial Trend ANOVAs did not reveal the hypothesised quadratic effects: movement planning time ($F(1,14) = 0.39, p = 0.55, \eta_p^2 = 0.03$); absolute error ($F(1,14) = 2.63, p = 0.13, \eta_p^2 = 0.16$); constant error ($F(1,14) = 0.99, p = 0.34, \eta_p^2 = 0.07$); variable error ($F(1,14) = 1.23, p = 0.28, \eta_p^2 = 0.08$). There were, however, significant linear effects for movement planning time ($F(1,14) = 4.88, p = 0.04, \eta_p^2 = 0.26$) and for variable error ($F(1,14) = 5.26, p = 0.04, \eta_p^2 = 0.27$). Inspection of the means revealed that participants were able to produce grip forces typically within 1 % MVC of their target, but with a slight bias to under-squeeze the handgrip dynamometer. Importantly, their movement planning times reduced, and they became more consistent from the pre-tests to the post-test,

providing evidence of improved movement planning and initiation across the Test phase (Figs. 4A - 4D).

Training Phase. Repeated measures Polynomial Trend ANOVAs revealed the expected significant linear effect for movement planning time ($F(1,14) = 14.32, p = 0.002, \eta_p^2 = 0.51$). This was characterized by an improvement in performance (i.e., shorter planning times) from neurofeedback training session 1 to training session 2, and again from training session 2 to training session 3 (Fig. 4A). There were no linear effects for absolute error ($F(1,14) = 0.84, p = 0.37, \eta_p^2 = 0.06$), constant error ($F(1,14) = 1.12, p = 0.31, \eta_p^2 = 0.07$) or variable error ($F(1,14) = 1.47, p = 0.25, \eta_p^2 = 0.10$).

All Visits. Six-level repeated measures ANOVAs to compare performances across all experimental visits revealed a significant effect for movement planning time ($F(5,70) = 4.40, p = 0.009, \eta_p^2 = 0.24, \epsilon = 0.61$). This was characterized by a significant linear trend ($F(1,14) = 9.04, p = 0.009, \eta_p^2 = 0.39$), with improvements in performance over the course of the experiment, and which were particularly evident during the training phase (Fig. 4A). There were no significant effects for absolute error ($F(5,70) = 1.87, p = 0.19, \eta_p^2 = 0.12, \epsilon = 0.26$), constant error ($F(5,70) = 1.65, p = 0.22, \eta_p^2 = 0.11, \epsilon = 0.24$) or variable error ($F(5,70) = 2.77, p = 0.07, \eta_p^2 = 0.16, \epsilon = 0.49$).

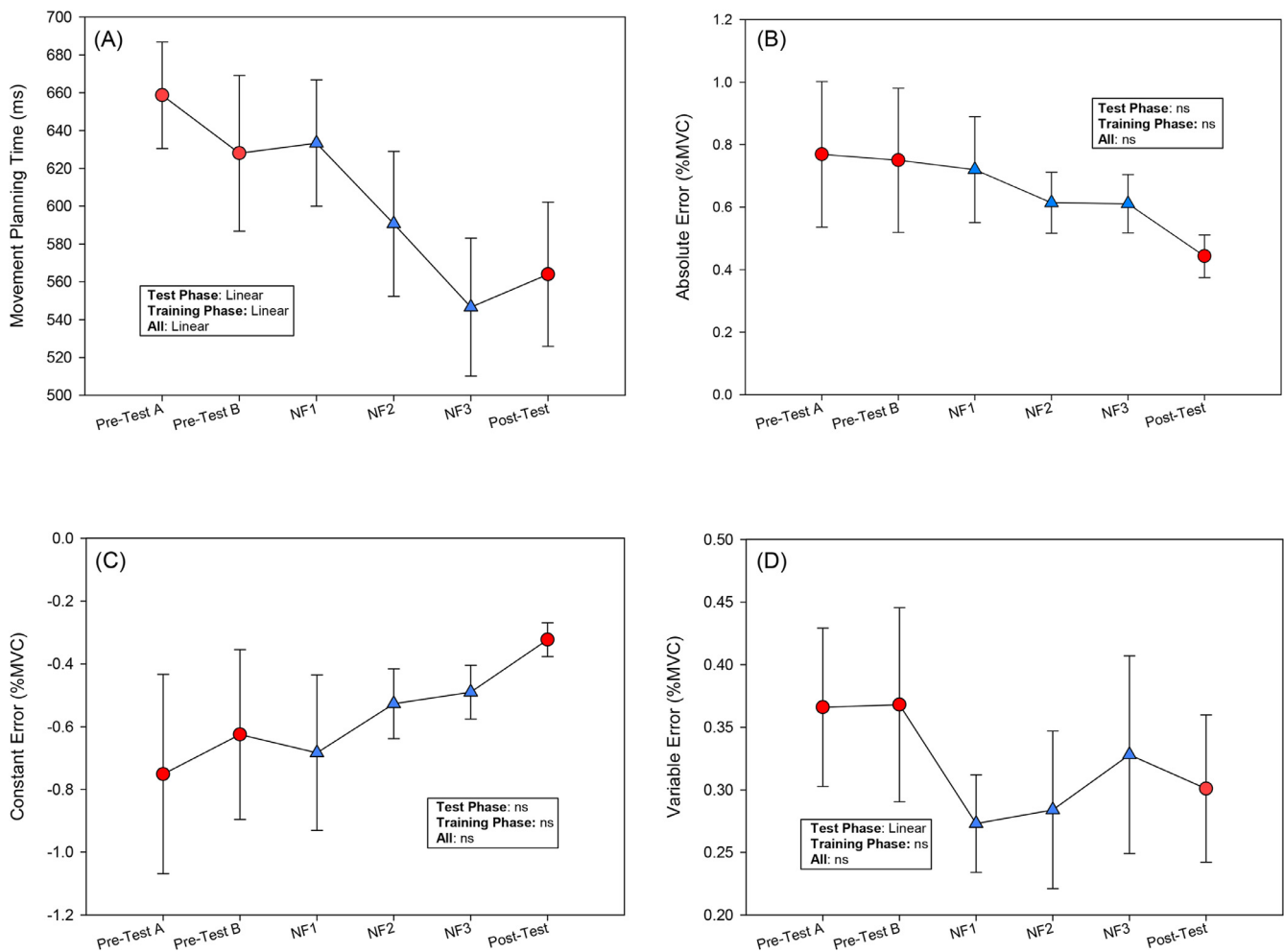


Fig. 4. Mean movement planning time (Panel A), absolute error (Panel B), constant error (Panel C), variable error (Panel D) and on the precision handgrip task. For movement planning time, smaller values indicate better performance. Absolute error reflects accuracy (i.e., proximity to target), constant error reflects bias (i.e., any tendency to undersqueeze or oversqueeze) and variable error reflects consistency – in all cases scores of zero (no error, no bias, strong consistency) is optimal. Pre-test A = on anti-Parkinsonian medication and before neurofeedback intervention. Pre-test B = off anti-Parkinsonian medication and before neurofeedback intervention. NF1, NF2 and NF3 = neurofeedback training sessions off anti-Parkinsonian medication. Post-test = off anti-Parkinsonian medication and after neurofeedback intervention. Error bars indicate standard error of the means. Note: Red circles indicate three data points analysed in the test phase. Blue triangles indicate three data points analysed in the training phase. All six datapoints were analysed in the “All” phase.

Table 2
MDS-UPDRS and PDQ-8 descriptive statistics.

Measure (range of possible scores) ^a	Pre-test A (on-medication)		Pre-test B (off-medication)		Post-test (off-medication)	
	M	SD	M	SD	M	SD
MDS-UPDRS Part II (MEDL) (0–52)	10.94	8.79	9.63	7.37	9.53	7.10
MDS-UPDRS Part III (motor examination) (0–132)	22.88	14.56	29.00	14.75	30.07	11.99
PDQ-8 (0–100)	18.36	15.13	20.12	17.04	17.50	13.92

^a Higher scores indicate more severe motor symptoms of PD (MDS-UPDRS) / reduced quality of life (PDQ-8).

MDS-UPDRS and PDQ-8. The mean scores for MDS-UPDRS Part II (motor aspects of experiences of daily living), the MDS-UPDRS Part III (motor examination) and the PDQ-8 are presented in Table 2. Polynomial trend ANOVAs revealed significant quadratic and linear trends for the MDS-UPDRS Part III, (Quadratic: $F(1,14) = 5.36, p = 0.04, \eta_p^2 = 0.28$; Linear: $F(1,14) = 8.28, p = 0.01, \eta_p^2 = 0.37$) with the effect sizes indicating that the linear trend was strongest. This effect was driven by the least severe symptomatology observed in the (on-medication) pre-test A, and most severe symptomatology observed in the (off-medication) post-test (Table 2). No significant trends emerged for the self-reported measures, MDS-UPDRS Part II (Quadratic: $F(1,14) = 0.71, p = 0.41, \eta_p^2 = 0.05$; Linear: $F(1,14) = 1.70, p = 0.21, \eta_p^2 = 0.11$), PDQ-8, (Quadratic: $F(1,14) = 1.09, p = 0.32, \eta_p^2 = 0.07$; Linear: $F(1,14) = 1.11, p = 0.31, \eta_p^2 = 0.07$).

Part B: qualitative

In response to the questions posed at the end of the neurofeedback training, 8 out of 15 participants (56 %) felt that they perceived some benefits of the neurofeedback training, while 13 out of 15 participants (86 %) indicated that they would recommend this type of neurofeedback training to other people with PD. Thematic content analyses identified three areas of perceived benefit: improved walking, improved psychological control, and improved motor control. These themes and some example comments related to each are presented in Fig. 5.

Reasons that participants offered to support their assertion that they would recommend this type of neurofeedback training to others included: “it is good to find non-pharmacological treatments, it empowers you”, “it is fun”, “having visual and auditory feedback is highly useful”, “it is interesting”, “controlling the alpha makes you able to control the subconscious” and finally, “because it works for me!”.

The final question, probing neurofeedback strategies, was explorative. In brief, 12 out of 15 participants (80 %) reported developing some helpful strategies to silence the neurofeedback tone (i.e., control their mu ERD). The most reported strategy was a combination of focus on the neurofeedback screen along with strategies to relax and clear the mind of anything else. These explorative data are reported in Supplementary Table 1.

Discussion

The primary goal of this experiment was to provide the first examination of the feasibility of home-based EEG mu neurofeedback training in people with PD. It represents a unique decentralised trial of a scalable, non-invasive, and personalised neuromodulation technique. Our target for neurofeedback training, mu ERD, was informed by previous research implicating mu ERD at central sites as key indices of movement efficacy in people with PD (e.g., [11,36,38]). Based on earlier reports from healthy controls, we hypothesised that EEG mu activity would be trainable [54] in a home setting. Our secondary aims were to shed light on the potential efficacy of neurofeedback as a candidate non-pharmacological treatment for the motor symptoms of PD (e.g., explore the comparative effects of neurofeedback versus pharmacological treatment on PD symptomatology). Finally, we used thematic content analyses to

qualitatively explore participants’ experience of this novel home-based EEG neurofeedback training.

Effects of neurofeedback on cortical activity

Based on our hypotheses, we expected that quadratic changes (test-phase) and linear changes (training-phase) in mu power would evidence learned self-regulation and endorse the feasibility of our neurofeedback treatment. EEG data during the test phase of the study confirmed the expected quadratic effect where mu power was greater (suggesting impaired ERD) in pre-test B (off-medication) than in pre-test A (on-medication) and post-test (off-medication) at the bilateral C3 and C4 sites. The difference between the pre-tests is in line with previous research that reported improved mu ERD before and during finger and hand movements when participants were on anti-Parkinsonian medication [13,36]. Importantly, our home-based EEG neurofeedback training appeared to enable people with PD to reduce their pre-movement mu power in the absence of medication (post-test). This finding is in line with previous work that demonstrated the trainability of EEG mu activity in healthy controls [49,54] and it provides encouraging evidence that EEG mu neurofeedback training can help people with PD to self-regulate their pre-movement cortical activity over the C3 (or C4) electrode position.

Data obtained during the training phase of the experiment provide further support for the efficacy of the intervention in training participants to self-regulate their cortical activity. Specifically, there was a linear effect for training session whereby mu power decreased (suggestive of greater ERD) from the first and second to the final neurofeedback training session. This could reflect some self-regulation of EEG activity generated by the primary motor cortex [65], a key region involved in encoding kinematic and muscle information of complex hand movements [30]. Previous attempts of motor imagery-based rt-fMRI neurofeedback training yielded effects that were mostly restricted to premotor areas [60,61], suggesting neurophysiological differences between imagery-based and pre-movement neurofeedback approaches. Mu power did not change significantly within each training session, although there was some evidence for within-session improvement indexed by more frequent silencing of the tone as each session progressed (supplementary Fig. 1). The different strength of between-session and within-session changes speak to a classic distinction between current performance and learning (for a review see [56]). In brief, within-session changes reflect current performance – improvement within a training session indicates a positive adaptation to the feedback. Learning, on the other hand, reflects a more enduring adaptation in the individual, and is evidenced by them starting a next session, on a subsequent day, at a better level than when they started the previous session. Many studies document within-session improvements, and then regression back to the original level in a subsequent session – this case illustrates short-term adaptation to feedback in the absence of longer-term learning [56]. Between-session (i.e., learning) effects, which can emerge with or in the absence of within-session effects, are most desirable as they reflect more stable benefits to the individual [56]. The current study provides evidence of learning, alongside some tentative evidence of within-session performance improvement. In addition to evidencing learned self-regulation,

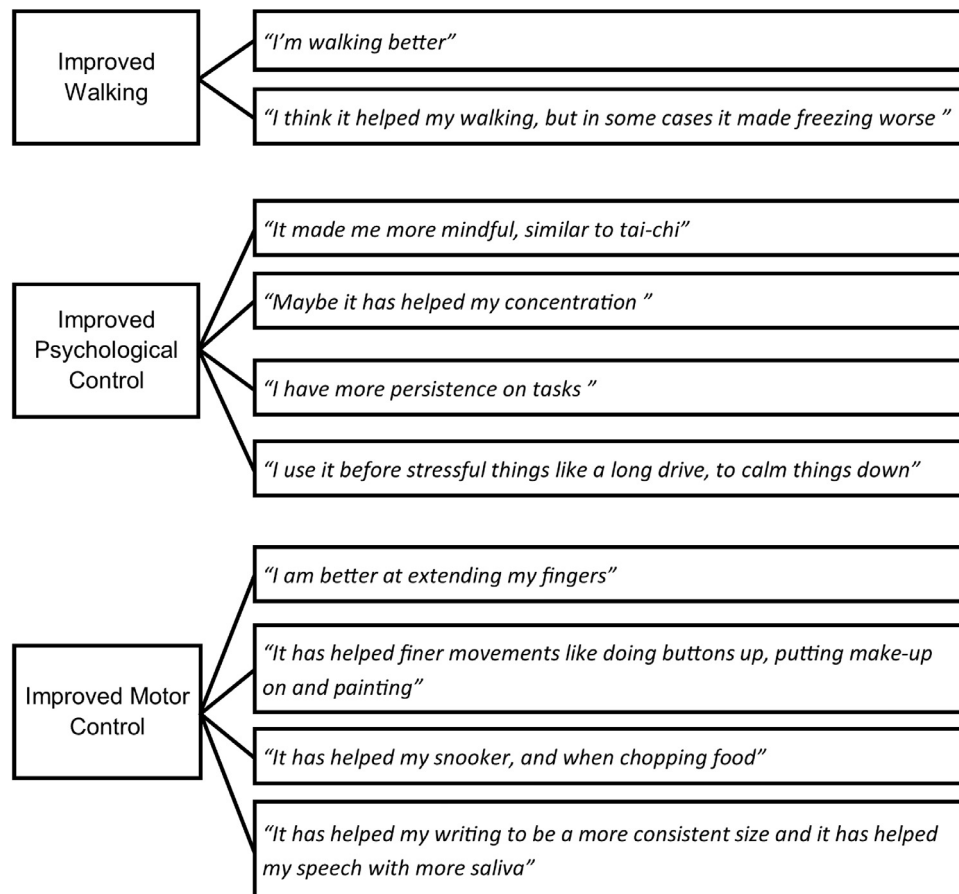


Fig. 5. Perceived benefits of neurofeedback training and example quotes from participants.

the greater relative strength of our between-session effects could additionally reflect, to some extent, participants being able to better distinguish changes in their brainwaves when the threshold for silencing the tone was most extreme (i.e., neurofeedback session 3). Sleep consolidation is likely to have further accelerated the between-session training benefits [37]. To capitalize on these effects, future research could implement a higher number of shorter duration training sessions, including stronger thresholds than applied here, and spread over a greater number of days.

In sum, the experiment provides very encouraging EEG data to reveal for the first time that participants with PD can use home-based neurofeedback to restore disrupted pre-movement mu activity to a degree that is comparable to the effects of pharmacological intervention (Fig. 3B-3C). We hence achieved our first aim, and our results provide the first confirmation of the feasibility of home-based neurofeedback training in PD.

Effects of neurofeedback on motor performance and PD symptomology

Our secondary outcomes concerned the effects of the neurofeedback treatment on measures of motor performance and PD symptomology. We expected our measures of precision handgrip performance to yield quadratic effects during the test phase of the experiment to index a worsening performance from pre-test A to pre-test B (reflecting the withdrawal of medication) and an improvement from pre-test B to post-test (reflecting benefits of neurofeedback training). Instead, we found linear improvements for movement planning time (all phases) and variable error (test phase), and no significant changes for absolute error and constant error. While not in line with our initial expectations, it is noteworthy that the clearest performance effects were the linear reductions in

movement planning time. Reduced movement planning time reflects improved performance due to superior pre-planning of force [26,27] and mu ERD is closely related to planning and initiation of movement [7]. One could attribute this performance improvement simply to practice. However, the improvements occurred when participants were off-medication, which has previously stifled learning [57]. Moreover, if practice were the complete explanation for our movement planning time results, we would expect to see similar practice effects across the other performance measures. The inconsistent improvement in variable error (i.e., limited to the test phase – Fig. 4D) and the absence of improvement across the absolute and constant error measures thereby challenges the practice effect interpretation. Instead, our findings indicate a selective effect of our neurofeedback protocol on movement planning, where benefits accrued from one neurofeedback training session to the next, and where some of those benefits were retained at post-test when the neurofeedback was withdrawn (Fig. 4A).

In line with this interpretation of the data, it is worth noting that our observer-rated, rather global behavioural measure of PD symptomology (MDS-UPDRS Part III), was unaffected by our intervention (i.e., similar symptomology in pre-test B and post-test). This adds further credence to the idea that benefits of our neurofeedback protocol were very specific to the planning of our target handgrip task. Finally, neither medication nor neurofeedback training resulted in a significant change in self-report measures related to motor aspects of daily living or quality of life. These measures ask respondents to complete the items in relation to their feelings over the past week (MDS-UPDRS Part II) and the past month (PDQ-8). This method of aggregate recall over time may have washed out the relatively transient increases in symptomatology that participants were experiencing (i.e., as captured in the MDS-UPDRS Part III) during the off-medication visits.

Participant experience of neurofeedback training

In addition to the quantitative data, we obtained brief qualitative data and vignettes to investigate participants' personal accounts and experience of our home-based intervention. These data indicate that the intervention was well-received. Just over half of the participants expressed that they perceived some benefit of the neurofeedback training, with the key themes being improved walking, improved psychological control (e.g., ability to concentrate and relax) and improved motor control (Fig. 5). In addition, nearly all participants (13/15) indicated that they would recommend EEG neurofeedback training to other people with PD. This suggests that most participants were pleased with the intervention, and this was backed up by comments indicating that the neurofeedback was "interesting", "empowering" and "fun". The lack of a control group makes it difficult to exclude the possibility of socially desirable responding that could have inflated the positive sentiment in the qualitative reports [51,58]. However, it is plausible that the home-based nature of the training did instil some genuine psychological benefits. For instance, in accord with the tenets of basic needs theory [52], the regular social interaction with the experimenter may have helped participants to fulfil the basic psychological need for relatedness. Learning to self-regulate brainwaves may enhance perceived psychological control and assist in satisfying basic needs for autonomy and competence. Furthermore, any combination of these factors can inflate perceived coping resources, allowing individuals to appraise situations (e.g., how one feels right now, with current symptomology), in more favourable ways [44]. Recent neurofeedback studies support these theoretical assertions, with successful self-regulation itself (e.g., with a relaxation technique) being shown to yield improvements for different mood states [40], which can occur with just a single training session [39]. This could explain why self-reported symptomology was similar at post-test (off-medication) compared to pre-test A (on-medication), even though observed symptomology at post-test was worse. In addition to the qualitative reports, it is also noteworthy that all but one participant completed the multi-session protocol, attesting to the potential for superior retention-rates of participants in decentralised compared to traditional clinical trials [50]. In sum, the views captured from our sample indicate that future home-based non-pharmacological interventions such as EEG neurofeedback are likely to be well received by people with PD.

Future directions

This feasibility study demonstrates the practicality and potential utility of home-based EEG neurofeedback training in PD and can provide a blueprint for future research to further interrogate EEG neurofeedback as a non-pharmacological PD treatment. We have already highlighted that future research would do well to replicate our experiment with a control group to better disentangle specific intervention benefits from those that may arise due to practice or socially desirable responding [51,58]. In addition, future neurofeedback research could consider providing training in augmentation to medication. For instance, honing self-regulation skills via neurofeedback while being on-medication may eventually allow a reduction in medication dosage, with the EEG entrainment supplementing the reduced dosage to yield equivalent motor outcomes. On the basis that medication can enhance learning [57], an on-medication state may enhance neurofeedback training success. Neurofeedback training success may further benefit from providing explicit strategies to guide participants in how to control the neurofeedback signal from the start [21]. In reporting strategies that participants identified by themselves in the present study (supplementary Table 1), we provide some useful starting points for future work.

While the present intervention impacted most clearly upon movement initiation, alternative neurofeedback protocols that focus on EEG activity during movement execution may be able to yield benefits to online control measures. For example, based on its inhibitory effects that can impair movement execution [32] protocols could provide continuous beta power feedback during skill execution instead of / in addition to using mu ERD

as the cue to initiate movement. Future neurofeedback protocols that target during movement control could employ wearable technologies to assess intervention effects on the execution of regular activities of daily living [59]. They could further record psychological factors related to mood, motivation and self-efficacy to evaluate their role as possible mediating factors of neurofeedback training benefits [38].

We encourage future efforts to continue to use the CRED-nf checklist [51] to ensure best practice guidelines are followed and rigorous experimental designs continue to be adopted. We also encourage researchers to continue to pre-register their trials and we hope that the documentation of this experiment will inform more detailed pre-registered study protocols in the future [17,46,53]. Lastly, while the present study focused on motor rehabilitation in PD, the shown proof-of-concept for a multi-session supervised neurofeedback experiment in a home-setting may encourage exploration of other clinical use cases. For instance, home-based neurofeedback training can target cognitive symptoms in neurodegenerative disorders [62] or mental diseases [63,5] or aim to facilitate movement in other rehabilitation contexts (e.g., recovery from stroke) [35]. Recent technical advances in mobile EEG [43] and optical neuroimaging methods such as functional near-infrared spectroscopy (fNIRS) [28,29] further expand the exciting prospects of mobile, ambulatory, home-based and even dyadic [31] neurofeedback applications.

Conclusion

This study provided the first examination of home-based EEG neurofeedback as a potential non-pharmacological, personalised intervention for people with PD. The results provide novel evidence to endorse the feasibility of home-based EEG neurofeedback training to help people with PD to self-regulate preparatory movement-related brain rhythms and serve as a scalable non-invasive, neuromodulatory intervention. Data further indicate that mu ERD neurofeedback may expedite the initiation and enhance the consistency of fine movements, but our results fall short of providing evidence for transfer benefits to online control of gross movements or wider symptomology reduction. Given the high acceptability and the clear feasibility of home-based neurofeedback in early-stage PD, we see considerable promise for neurofeedback as a non-pharmacological treatment. Larger-scale investigations of neurofeedback in people with PD are warranted and we believe that this founding work can provide a significant blueprint for those future research endeavours.

Data statement

The datasets analysed are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.neucli.2024.102997](https://doi.org/10.1016/j.neucli.2024.102997).

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